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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/765,026	01/13/97	BARKATS	ST94051-US

EXAMINER: M

HM11/0706

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ART UNIT	PAPER NUMBER
1636	9

DATE MAILED: 07/06/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 4/6/98.

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three (3) month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 47 and 61-82 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 47 and 61-82 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-410-238/40050

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 47, 61-65, 67 and 69-81 are rejected under 35 USC 103(a) as being unpatentable over Coyle et al. in view of Greenberger.

Applicants claim a method for treating diseases such as ALS, Parkinson's disease (PD), hypertension, etc., wherein said diseases are characterized by an excess of free radicals, said

method comprising administering to patients a replication defective adenovirus encoding a superoxide dismutase operatively linked to a promoter enabling expression in a target cell.

Coyle et al. (Science, Vol. 262, 29 Oct. 1993, pp. 689-695, see whole article, particularly pp. 689-690 and 694) recites the role played by free radicles in diseases such as ALS, PD, etc., reviews the well known roles of the different forms of SODs in reducing the levels of free radicals and the possible correlation between reduction or lose of CuZnSOD activity with diseases such as ALS in humans. Coyle et al. does not teach the use of adenovirus vectors to deliver SODs to target cells so as to reduce the levels of free radicals and therefore treat diseases in which said free radicals may play a role.

Greenberger (U.S. Patent 5,599,712, See whole document, particularly Figs. 3a-3b, the paragraph bridging Columns 5-6, Columns 7-8, paragraph bridging Columns 11-12, Columns 13 and 16) teaches the generation of replication defective adenoviral vectors capable of expressing human SODs (i.e. MnSOD or CuZnSOD, etc. derived from genomic or cDNA sources) wherein the SOD gene is under control of a viral (i.e. the adenoviral MLP) promoter, human cells which are infected with said vectors and pharmaceutical compositions comprising said vectors. The vectors serve to reduce the level of free radicals in target cells.

The ordinary skilled artisan, seeking to treat diseases which are characterized by an excess of free radicals would have been motivated to use the teachings of Coyle et al. on the role of excess free radicals in disease conditions such as PD and ALS and the possible correlation between reducing said levels of excess free radicals and alleviating disease conditions combined with the

teachings of Greenberger on the generation of recombinant adenoviral vectors designed for the delivery of SODs to target cells wherein said adenoviral vectors are designed to reduce the levels of free radicals and thereby reduce the levels of cell damage due to said free radicals so as to use said adenoviral vectors to treat diseases characterized by an excess of free radicals. It would have been obvious for the skilled artisan to do this because Coyle et al. indicates that a reduction in the levels of free radicals can alleviate some human diseases characterized by excess free radical levels. Given the teachings of the cited prior art references, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 66 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coyle et al. in view of Greenberger and Engelhardt et al.

Coyle et al. is cited as in the above 35 USC 103(a) rejection.

Greenberger (U.S. Patent 5,599,712), is cited as in the above 103(a) rejection. Greenberger does not recite the generation of adenoviral vectors containing non-functional E2, E4, etc. genes.

Engelhardt et al. (PNAS, Vol. 91, June 1994, pp. 6196-6200, see whole article, particularly the Abstract and last three paragraphs of the Discussion) teaches the use of adenoviral vectors containing a non-functional E2 gene. It is noted that PNAS Volume 91 was received in the U.S. Patent Office Biotechnology Library on June 27, 1994. Coyle et al. and Greenberger teach the basic aspects of the claimed invention absent the use of adenoviral vectors comprising inactivated

or nonfunctional additional adenoviral genes such as the E2 gene. Since Engelhardt et al. teaches the desirability of using adenoviral vectors wherein the E2 gene is non-functional (i.e. said vectors result in improved transgene persistence and reduced inflammatory responses), it must be considered that the ordinary skilled artisan, seeking to generate an adenoviral vector for the expression of SOD, would have been motivated to use an adenoviral vector wherein the E2 gene is non-functional for the express, art recognized, desirability of using these vectors (i.e. generating an adenoviral vector construct desirable for use in gene therapy). It would have been obvious for the ordinary skilled artisan to use an adenoviral construct lacking a functional E2 gene because of the desirability (as disclosed by Engelhardt et al.) of using such a vector for gene therapy. Given the teachings of the cited prior art references and absent evidence to the contrary, it must be considered that the claimed invention would have been *prima facie* obvious to the ordinary skilled artisan and that said artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Coyle et al. in view of Greenberger and Le Gal La Salle et al.

Coyle et al. and Greenberger are applied as in the above 35 USC 103 rejections. Neither Coyle et al. nor Greenberger teach the use of the RSV-LTR promoter to drive expression of a heterologous gene in an adenovirus vector.

Le Gal La Salle et al. (Science, Vol. 259, 12 Feb. 1993, pp. 988-990, see whole article, particularly p. 988) recites the use of the RSV-LTR promoter in the context of driving expression of heterologous genes in recombinant adenoviruses.

Coyle et al. and Greenberger teach the essential aspects of the invention with the exception of using the RSV-LTR promoter to drive expression of the SOD gene. However, Le Gal La Salle et al. teach the use of the RSV-LTR promoter to drive expression of heterologous genes in a recombinant adenovirus expression vector. The ordinary skilled artisan, therefore, would have been motivated to use the RSV-LTR promoter for the express purpose of driving expression of the heterologous gene (i.e. the SOD gene) since Le Gal La Salle et al. specifically recites using the RSV-LTR promoter to drive expression of a heterologous gene in the context of a replication defective recombinant adenovirus vector. It would have been obvious for the ordinary skilled artisan to use this promoter because it is a well known promoter which has been used in the prior art (Le Gal La Salle et al.) to drive expression of heterologous genes in the context of a recombinant replication defective adenovirus vector. Given the teachings of the cited prior art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 47 and 61-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 (and dependent claims) are vague in the recitation of the phrase "...capable of regulating..." since the capacity of a compound or composition to perform some function is merely a recitation of a latent characteristic of said compound or composition and said language carries no patentable weight. Redrafting the claim to delete the phrase "that is capable of regulating" and substituting --which regulates-- would be remedial.

No Claims are allowed.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David Guzo
July 6, 1998

DAVID GUZO
PRIMARY EXAMINER